

REMARKS

Entry of this Response and Amendment is proper under 37 C.F.R. § 1.116, because the response places the application in condition for allowance for the reasons discussed below; raises no new issue requiring further search and/or consideration, as the remarks amplify issues previously discussed throughout prosecution; presents no additional claims; and places the application in better form for an appeal, if necessary. Entry of the response, reexamination, and reconsideration in light of the following remarks are thus respectfully requested.

1. Status of the Claims

The status of the claims following entry of the amendment is as follows:

Claims canceled: None

Claims pending: Claims 1-31

Claims allowed: None

Claims rejected: Claims 1-7, 9, 11-24, 26, and 28-31¹

Claims objected: Claims 8, 10, 25, and 27

2. Support for the Amendments

The amendment to claim 1 is supported *ipsis verbis* in claim 2 (first promoter “is used to express a male sterility gene in corresponding male sterile plants”). The amendment is further supported in the specification at least at page 23, lines 1-11, e.g., line 7, which discloses expression from a second “tapetum-specific promoter” (e.g., A9 promoter) that “begins earlier” than a first “tapetum-specific promoter” (e.g., TA29 promoter):

since the tapetum-specific promoters used to transcribe the barstar gene have overlapping expression profiles, accumulation of barstar protein in tapetal tissues begins earlier (from the A9 promoter) than barnase (which is under transcriptional control of the TA29 promoter). . . .

The amendment to method claim 16 combines steps (i) and (ii). The amendments to the construct used in claim 16 are supported for the same reasons as the amendments to claim 1.

¹ The Office Action Summary incorrectly lists the rejected claims as 1-7, 9, 11-24, 26, 31, and 38. Clarification is requested in the Office’s next communication.

The remaining amendments clarify the language of the claims or comport more closely with U.S. practice. No impermissible new matter is entered by the amendments.

The amendments are made solely to expedite prosecution and without concession that any ground of rejection is proper. The amendments thus are made without prejudice or disclaimer of Applicants' rights to pursue any and all disclosed subject matter in this application or in a continuing application.

3. Acceptance of the Drawings

Applicants note with appreciation the indication that the drawings filed on January 6, 2006, are acceptable.

4. Request Regarding Vacated Notice of Non-Compliant Amendment

Applicants appreciate the Examiner's indication that the Notice of Non-Complaint Amendment mailed November 17, 2008 was vacated. PAIR, however, still reflects the entry of a Notice of Non-Compliant Amendment issued November 17, 2008. When the Office audits Patent Term Adjustments (PTA) upon allowance, it bases its audit on PAIR entries and assumes that PAIR entries are correct. The Office's PTA audit will incorrectly record Applicant delays, unless the PAIR entry is corrected to reflect the Notice's vacated status. Accordingly, Applicants request the PAIR entry be changed to "Miscellaneous Communication" or some other suitable entry.

5. Indication of Allowable Subject Matter

Applicants appreciate the indication that claims 8, 10, 25, and 27 are free of the cited art and would be allowable if rewritten as independent claims.

6. Rejections under 35 U.S.C. § 103(a)

The Combination of Flasinski, Fabijanski, and Shah

Claims 1-2, 5-6, and 11-15 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over U.S. Published Application No. 2006/0191038 A1 ("Flasinski") in view of U.S. Patent No. 6,162,964 ("Fabijanski") and further in view of Shah *et al.*, *Proc. Nat'l Acad. Sci. USA* 79: 1022-1026 (1982) ("Shah").

Applicants traverse the rejection. The Office fails to establish *prima facie* obviousness. Further, the Office improperly limits the showing of unexpected results to one exemplified embodiment using an A9 promoter, shown in the examples of the specification. While evidence of unexpected results must be commensurate in scope with the claims, patentability can be established by a showing of unexpected superiority for *representative* compounds within the scope of the claims. What is representative is decided on a case-by-case basis.²

GROUND S FOR REJECTION

The primary reference, Flasiński, generally discloses plant promoters over almost four columns of text (¶¶ 178, 219-230), which contains the following sole mention of male pollen-specific promoters:

[0224] A maize pollen-specific promoter has been identified in maize. Other genes specifically expressed in pollen have been described. (Parentheticals omitted.)

Flasiński also incorporates over three dozen U.S. patents by reference to disclose genes conferring traits of interest. One of these patents, one (U.S. Patent No. 5,689,041) discloses hybrid seen production using promoter expressed in male reproductive tissue.

The Office relies on Fabijanski for motivation to select from Flasiński's vast genus of promoters those promoters with overlapping temporal expression patterns in male reproductive tissues. Fabijanski discloses "pollen specific promoters," including pollen specific promoters from *Brassica napus* (col. 13, lines 15-18 and 36-37). Pollen specific promoters may limit the duration of gene expression to the period of pollen formation in the plant (col. 13, lines 19-23 and 37-42). In particular, Fabijanski discloses four structurally distinct *B. napus* promoters, L4, L10, L16 and L19, having overlapping temporal expression patterns in male reproductive tissues

² See *Ex parte Winters*, 11 USPQ2d 1387, 1388 (Bd. Pat. App. & Int. 1989) (emphasis in original):

Certainly, objective evidence of nonobviousness must be commensurate in scope with the claims which the evidence is offered to support. See *In re Boesch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980); *In re Greenfield*, 571 F.2d 1185, 197 USPQ 227 (CCPA 1978); *In re Tiffin*, 443 F.2d 394, 170 USPQ 88 (CCPA 1971). By the same token, appellant is not required to test each and every species within the scope of the appealed claims and compare same with the closest prior art species. Rather, patentability is established by a showing of unexpected superiority for *representative* compounds within the scope of the appealed claims. What is representative is a factual question which is decided on a case-by-case basis.

See also M.P.E.P. § 2145, ¶ 9.

(col. 13, lines 24-31; col. 14, lines 4-10 and 19-28). As Applicants understand the rejection, the Office alleges it would have been obvious to use Fabijanski's promoters in Flasiński's constructs. Finally, the Office cites Shah for the proposition that it would have been allegedly obvious to use an actin gene sequence as the male fertility-restoring gene sequence.

ARGUMENT

1. The Office has not established *prima facie* obviousness.

The Office fails to establish *prima facie* obviousness for the following reasons. Flasiński fails entirely to teach or suggest combinatorial use of a first and second promoter with overlapping temporal expression profiles in tapetal tissues to control the expression of two different coding sequences of a fertility restorer gene, as recited. Nor does the Office make a case that Flasiński suggests such a combinatorial use of the two recited promoters.

Instead, the Office alleges that Fabijanski would have suggested the missing claim element. Fabijanski, however, provides alternative promoters that could be used by themselves (i.e., L4 **or** L10 **or** L19) to control tissue-specific expression of a male-sterility inducing gene. The Office indeed acknowledges that Fabijanski specifically discloses using the *same* promoter to control the expression of a male-sterility gene and a male-fertility (restorer) gene. *See* Office Action mailed March 18, 2009, at page 8, lines 1-2. Thus, Fabijanski, like Flasiński, fails to teach or suggest the combinatorial use of a first and second promoter with overlapping temporal expression profiles in male reproductive tissues to control the expression of two different coding sequences of a fertility restorer gene, as recited.

One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. MPEP § 2145 (citing *In re Keller*, 642 F.2d 413, 208 U.S.P.Q. 871 (C.C.P.A. 1981)). However, *neither* Flasiński nor Fabijanski teach or suggest the claim element of a combinatorial use of a first and second promoter with overlapping temporal expression profiles in male reproductive tissues to control the expression of two different coding sequences of a fertility restorer gene, as recited. "[O]bviousness requires a suggestion of all limitations in a claim." *CFMT, Inc. v. Yieldup Intern. Corp.*, 349 F.3d 1333, 1342, 68 U.S.P.Q.2d 1940 (Fed. Cir. 2003) (citing *In re Royka*, 490 F.2d 981, 985, 180 U.S.P.Q.

580, 583 (C.C.P.A. 1974)). The Office has not met this prerequisite in the present case. The rejection accordingly is unsubstantiated by evidence and must be withdrawn.

2. The claimed subject matter provides unexpectedly superior results.

Even if the Office could establish *prima facie* obviousness, for the sake of argument, the Office must weigh secondary evidence for non-obviousness. See, e.g., *Graham v. John Deere Co.*, 383 U.S. 1, 148 U.S.P.Q. 459 (1966). In the present case, the claimed subject matter provides unexpectedly superior results.

In the presently claimed construct and methods, different tapetum-specific promoters have overlapping temporal expression patterns in plant male reproductive tissues. Both promoters control the expression of fertility restorer genes (e.g., *barstar*). The specification (e.g., page 23, lines 1-11) discloses the use of a representative construct having the general structure:

A9-fertility restorer gene::TA29-fertility restorer gene (e.g., [A9-bs(fm)::TA29-bs(wt)]).

In this example, TA29 is a “first promoter,” and A9 is a “second promoter.” This construct is used to restore male fertility in a corresponding male sterile plant that comprises a construct having the general structure:

First promoter (e.g., TA29)-male sterility gene (e.g., *barnase*).

The presently claimed construct confers unexpectedly superior results. When restoring fertility with the construct above,

the frequency of fertile plants registered a substantial increase to 89.8% indicating that *barstar* levels are significantly higher as compared to the earlier (control) constructs (p. 23, lines 1-3).

The specification teaches that the frequency of fertile plants substantially increases, because the second promoter (e.g., A9) expresses earlier than the first promoter (e.g., TA29). This allows fertility restorer protein to accumulate before the male sterility gene is expressed:

Since the tapetum-specific promoters used to transcribe the *barstar* gene have overlapping expression profiles, accumulation of *barstar* protein in tapetal tissues begins earlier (from the A9 promoter) than *barnase* (which is under transcriptional control of the TA29 promoter) and continues during the entire period when

barnase is expressed (from the TA29-*barstar* cassette). Extended expression of the *barstar* gene therefore builds up a reservoir of the inhibitor protein which ensures effective inhibition of barnase (p. 23, lines 5-11).

The improved fertility depends on the temporal expression pattern of the first and second promoters. For this reason, the same substantial increase in male fertility would be expected if a different combination of restorer gene and male sterility gene were used. It also follows that other promoters can be used to obtain the same result, provided the temporal expression pattern of the first and second promoters is the same. To obtain the same results, the second promoter (e.g., A9) expresses earlier than the first promoter (e.g., TA29), allowing the fertility restorer protein to accumulate before the male sterility gene was expressed from the corresponding first promoter (e.g., a TA29-*barnase* construct). This relationship between the first and second promoters is reflected in the present claim language:

wherein said first and second tapetum-specific promoters have overlapping temporal expression patterns in male reproductive tissues of said crop plants,

wherein said first tapetum-specific promoter is used to express a male sterility gene in a corresponding male sterile plant, and

wherein expression from said second tapetum-specific promoter begins earlier than said first tapetum-specific promoter.

The evidence of unexpected results thus is commensurate in scope with the claims. The disclosed constructs using the TA29 and A9 promoters are *representative* constructs within the scope of the claims. The evidence shows that other constructs would exhibit the same unexpected superiority. Accordingly, the entire scope of the claimed subject matter is patentable over the combination of references. *See Ex parte Winters*, 11 USPQ2d at 1388. The rejection should be withdrawn and the claims allowed.

The Combination of Flasinski, Fabijanski, Jofuku and Stevenson

Claims 1-6 and 11-15 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Flasinski in view of Fabijanski, further in view of Jofuku *et al.*, *Plant Cell* 1: 1079-93 (1989) ("Jofuku") and Stevenson *et al.*, *Nucl. Acids Res.* 14: 8307-30 (1986) ("Stevenson").

Applicants traverse the rejection. The Office applies the combined references to suggest modifying the construct allegedly suggested by the combination of Flasinski and Fabijanski. Specifically, the Office combines the teachings of Jofuku and Stevenson to suggest a construct

comprising a male sterility gene encoding a protease, such as trypsin, and a male fertility restorer gene encoding a protease inhibitor, such as trypsin inhibitor. Applicants do not concede that the Office has established *prima facie* obviousness for at least the reasons above. In particular, Jofuku does not remedy the deficiencies in the combination of Flasinski and Fabijanski noted above. In any event, the claimed subject matter provides unexpectedly superior results compared to the constructs and methods allegedly suggested by the combined references for the reasons above. The rejection accordingly should be withdrawn.

The Combination of Flasinski, Fabijanski, Williams, and Michiels

Claims 1-7, 9, 11-24, 26, and 28-30 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Flasinski in view of Fabijanski and further in view of U.S. Patent No. 5,750,867 ("Williams") and U.S. Patent No. 6,372,960 ("Michiels").

Applicants traverse the rejection. The teachings of Flasinski and Fabijanski and their deficiencies are set forth above. Williams teaches a construct comprising a fertility restorer gene sequence operably linked to a promoter, such as the TA29 promoter. The Office particularly points to the teaching in Williams of a *barstar* sequence essentially identical to the recited sequence of SEQ ID NO: 1. Michiels teaches a codon-optimized variant of a *barstar* gene. The Office alleges it would have been obvious to use both *barstar* gene sequences in the construct suggested by the combination of Flasinski and Fabijanski for the reasons above.

Applicants do not concede that the Office has established *prima facie* obviousness. In particular, Williams, like Flasinski and Fabijanski, does not teach or suggest the claim element of a combinatorial use of a first and second promoter with overlapping temporal expression profiles in male reproductive tissues to control the expression of two different coding sequences of a fertility restorer gene, as recited. In any event, the claimed subject matter provides unexpectedly superior results compared to the constructs and methods allegedly suggested by the combined references for the reasons above. Without a teaching of all the limitations and an expectation that the combined elements would work, obviousness cannot be adduced. The rejection accordingly should be withdrawn.

CONCLUSION

The claims are believed ready for allowance. If there are any other fees due in connection with the filing of this Amendment, please charge the fees to our Deposit Account No. 50-0573. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account. If an Appeal Fee is required to maintain pendency of the present application, the Office is authorized to charge the Appeal Fee and use this paper as a Notice of Appeal.

Respectfully submitted,

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